

- B<sup>1</sup>
- a) inhibiting the proliferation of smooth muscle cells in vivo;
  - b) stimulating the differentiation of smooth muscle cells in vivo;
  - c) regulating the migration of smooth muscle cells in vivo; and
  - d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC50/EC50 for at least one of said biological activities that is less than or equal to  $10^{-3}$ .

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2. **(Reiterated)** The pharmaceutical composition of claim 1 wherein said elastin-based composition is soluble and has an IC50/EC50 for each of said one or more biological activities that is less than or approximately equal to  $10^{-3}$ .

B<sub>2</sub> Sub C1 10<sup>-15</sup> 3. **(Amended)** The composition of claim 1 or 2 wherein said IC50/EC50 is greater than

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4. **(Reiterated)** The composition of claim 1 wherein said pharmaceutical composition provides a dose of said elastin-based composition equivalent to  $10^{-8}$  M of a peptide having the amino acid sequence of SEQ ID NO:2 at said target site.

Sub C1 6. **(Amended)** The composition of claim 1 wherein said elastin-based composition comprises a recombinant polypeptide.

B<sub>3</sub> 7. **(Amended)** The composition of claim 1 wherein said elastin-based composition comprises a synthetic peptide.

8. **(Amended)** The composition of claim 7 wherein said synthetic peptide comprises at least two repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).

9. **(Amended)** The composition of claim 8 wherein said synthetic peptide comprises 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).

10. **(Reiterated)** The composition of claim 1, wherein said elastin-based composition is crosslinked, precipitated, or coacervated.

11. **(Reiterated)** The composition of claim 1 wherein said elastin-based composition comprises an elastin matrix produced from a blood vessel.

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SUB  
C1 } 12. **(Amended)** The composition of claim 1 wherein said elastin-based composition is attached to a biocompatible support or biocompatible matrix.

13. **(Amended)** The composition of claim 12 wherein said biocompatible support or biocompatible matrix comprises a tube.

14. **(Amended)** The composition of claim 13 wherein said elastin-based composition is attached to an outer surface of said tube and additionally comprises a sheath encircling said tube.

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SUB  
C1 } 22. **(Twice Amended)** A method for prophylaxis or treatment of a disorder having diminished capacity to regulate smooth muscle cell function comprising delivery of the elastin-based composition provided by the pharmaceutical composition of claim 1 to said site of diminished capacity to regulate smooth muscle cell function.

23. **(Amended)** The method of claim 22 wherein said IC50/EC50 is greater than about  $10^{-15}$ .

24. **(Reiterated)** The method of claim 22 wherein said pharmaceutical composition provides a dose of said elastin-based composition equivalent to  $10^{-8}$  M of a peptide having the amino acid sequence of SEQ ID NO:2 at said target site.

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SUB  
C1 } 26. **(Amended)** The method of claim 22 wherein said elastin-based composition comprises a recombinant polypeptide.

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27. **(Amended)** The method of claim 22 wherein said elastin-based composition comprises a synthetic peptide comprising 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).

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28. **(Reiterated)** The method of claim 22 wherein said elastin-based composition is crosslinked, precipitated, or coacervated.

29. **(Reiterated)** The method of claim 22 wherein said elastin-based composition comprises an elastin matrix produced from a blood vessel.

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C1 }  
30. **(Amended)** The method of claim 22, wherein said elastin-based composition is attached to a biocompatible support or a biocompatible matrix.

31. **(Amended)** The method of claim 30 wherein said biocompatible support or biocompatible matrix comprises a tube.

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33. **(Reiterated)** The method of claim 22 wherein delivery comprises intravascular delivery of said elastin-based composition directly to a vascular site.

34. **(Reiterated)** The method of claim 33 wherein said disorder is selected from the group consisting of atherosclerosis, restenosis, vascular bypass graft stenosis, transplant arteriopathy, aneurysm, and dissection.

35. **(Reiterated)** The method of claim 22 wherein said elastin-based composition is delivered to and maintained at said site.

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C1 }  
B8 }  
36. **(Amended)** The method of claim 35 wherein said pharmaceutical composition is a tubular elastin-based composition and said method comprises using said pharmaceutical composition as a blood vessel.

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37. (Amended) The method of claim 36 wherein said blood vessel is used for vascular bypass.

38. (Amended) The method of claim 37 wherein said blood vessel is used for coronary artery bypass grafting.

39. (Amended) A method comprising implanting the pharmaceutical composition of claim 1 at a target site, wherein said target site is selected from the group consisting of the common bile duct, a pancreatic duct, the esophagus, the trachea, the urethra, the bladder, the uterus, and an ovarian duct.

[ Please add the following new claims: ]

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B9  
48. (New) The pharmaceutical composition of claim 1, wherein said elastin-based composition comprises a polypeptide having an amino acid sequence at least 90% identical to SEQ ID NO: 2, SEQ ID NO: 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells in vivo;
- b) stimulating the differentiation of smooth muscle cells in vivo;
- c) regulating the migration of smooth muscle cells in vivo; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC<sub>50</sub>/EC<sub>50</sub> for at least one of said biological activities that is less than or equal to 10<sup>-3</sup>.

49. (New) The pharmaceutical composition of claim 48, wherein said elastin-based composition comprises a polypeptide having an amino acid sequence identical to SEQ ID NO: 2, SEQ ID NO: 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID NO: 1.

50. (New) The pharmaceutical composition of claim 1, wherein said elastin-based composition is derivatized by linkage to one or more additional chemical groups for promoting sustained release.

39 51. (New) A method for prophylaxis or treatment of obstructive vascular disease, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease obstruction of a vessel, wherein said elastin-based composition is delivered to the site of vessel obstruction.

52. (New) A method for prophylaxis or treatment of vascular stenosis, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease vascular stenosis, wherein said elastin-based composition is delivered to the site of vascular stenosis.

53. (New) A method for prophylaxis or treatment of stenosis, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease stenosis, wherein said elastin-based composition is delivered to the site of stenosis, and wherein said site is selected from the group consisting of common bile duct, pancreatic duct, esophagus, trachea, urethra, bladder, uterus, and ovarian duct.

54. (New) A method for decreasing restenosis following angioplasty or bypass grafting, comprising delivering an amount of the elastin-based composition of claim 1 effective to decrease restenosis following angioplasty or bypass grafting, wherein said elastin-based composition is delivered to the site of restenosis.

55. (New) The composition of claim 1, wherein the elastin-based composition is a hexapeptide having the sequence represented in SEQ ID No: 1.

56. (New) The composition of any of claims 1, 2, 8, 9 or 55, where said elastin-based composition is dissolved or suspended within a biocompatible polymer matrix, which matrix permits diffusion of the elastin-based composition, to form a sustained-release composition.

57. (New) The composition of claim 56, wherein the biocompatible polymer matrix is selected from the group consisting of polyester, a polylactide, degradable lactic acid-glycolic acid copolymers, and poly-D-(-) hydroxybutyric acid.

58. (New) The composition of claim 56, wherein the biocompatible polymer matrix is formulated for coating an implantable medical device.

59. (New) The composition of claim 56, wherein the biocompatible polymer matrix is formulated for coating a stent.

*The claims presented above incorporate changes as indicated by the marked-up versions below.*

1. (Amended) A pharmaceutical composition that provides an elastin-based composition for localized delivery in vivo to a target site in vivo, said elastin-based composition comprising a polypeptide having an amino acid sequence at least 80% identical to SEQ ID NO: 2, SEQ ID NO: 3 ~~one or more elastic fibers, elastins, tropoelastins, or a peptide fragment-fragments~~ thereof including at least one hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has ~~and having~~ one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells in vivo;
- b) stimulating the differentiation of smooth muscle cells in vivo; ~~and~~
- c) regulating the migration of smooth muscle cells in vivo; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC50/EC50 for at least one of said biological activities that is less than or equal to  $10^{-3}$ .

3. (Amended) The composition of claim 1 or 2 wherein said IC50/EC50 ~~EC50/IC50~~ is greater than ~~or approximately equal to~~  $10^{-15}$ .

6. (Amended) The composition of claim 1 wherein said elastin-based composition comprises a recombinant polypeptide ~~tripeptide~~.
7. (Amended) The composition of claim 1 wherein said elastin-based composition comprises a synthetic elastin peptide.
8. (Amended) The composition of claim 7 wherein said synthetic elastin peptide comprises at least two repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
9. (Amended) The composition of claim 8 wherein said synthetic elastin peptide comprises 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
12. (Amended) The composition of claim 1 wherein said elastin-based composition is attached to a biocompatible support or biocompatible matrix.
13. (Amended) The composition of claim 12 ~~14~~ wherein said biocompatible support or biocompatible matrix comprises a tube.
14. (Amended) The composition of claim 13 ~~12~~ wherein said elastin-based composition is attached to an outer surface of said tube and additionally comprises ~~comprising~~ a sheath encircling said tube.
22. (Twice Amended) A method for prophylaxis or treatment of a disorder having ~~characterized by~~ diminished capacity to regulate smooth muscle cell function comprising delivery of the elastin-based composition provided by the pharmaceutical composition of claim 1 to said ~~target site~~ of diminished capacity to regulate smooth muscle cell function.
23. (Amended) The method of claim 22 wherein said IC50/EC50 ~~EC50 is less than or approximately equal to that of a peptide having the amino acid sequence of SEQ ID NO:2 and is~~ greater than about 10<sup>-15</sup> ~~1 nM~~.

26. (Amended) The method of claim 22 wherein said elastin-based composition comprises a recombinant polypeptide ~~tropoelastin~~.
27. (Amended) The method of claim 22 wherein said elastin-based composition comprises a synthetic ~~elastin~~ peptide comprising 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
30. (Amended) The method of claim 22, wherein said elastin-based composition is attached to a biocompatible support or a biocompatible matrix.
31. (Amended) The method of claim 30 wherein said biocompatible support or biocompatible matrix comprises a tube.
36. (Amended) The method of claim 35 wherein said pharmaceutical composition is a tubular elastin-based composition and said method comprises using said pharmaceutical composition as ~~an artificial~~ a blood vessel.
37. (Amended) The method of claim 36 wherein said ~~artificial~~ blood vessel is used for vascular bypass.
38. (Amended) The method of claim 37 wherein said ~~artificial~~ blood vessel is used for coronary artery bypass grafting.
39. (Amended) A method comprising implanting the pharmaceutical composition of claim 1 at a target site, wherein said target site is selected from the group consisting of the common bile duct, a pancreatic duct, the esophagus, the trachea, the urethra, the bladder, the uterus, and an ovarian duct.